

## PATENT ABSTRACTS OF JAPAN

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(71)Applicant : F I CORPORATION:KK

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(72)Inventor : SHIOTANI TOMOAKI

## (54) PROPOLIS PRODUCT HAVING ANTIOXIDANT ACTIVITY

## (57)Abstract:

PROBLEM TO BE SOLVED: To provide a propolis product having a wide range of biological activity of the propolis and an antioxidant activity effective for prevention and improvement of aging change.

SOLUTION: This propolis product having antioxidant activity comprises a mixture of extracts of the propolis obtained by extracting a clump of the raw propolis with two or more kinds of aqueous solutions of ethanol having different concentration of water, preferably the propolis extract is obtained by extracting the raw propolis with an aqueous ethanol solution including 5-10 vol.% of water and the extract obtained by extracting with an aqueous ethanol solution including 45-55 vol.% of water and then mixing both in a volumetric mixing ratio of 4-6:6-4. The propolis product having antioxidant activity preferably uses the clump of the raw propolis originating from Brazilian growth eucalyptus/rosemary.

## LEGAL STATUS

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JAPANESE

[JP,2002-306092,A]

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CLAIMS	DETAILED DESCRIPTION	TECHNICAL FIELD	PRIOR ART	EFFECT OF THE INVENTION	TECHNICAL PROBLEM
MEANS	EXAMPLE				

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[Translation done.]

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CLAIMS

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[Claim(s)]

[Claim 1] The antioxidation activity propolis product characterized by coming to mix the propolis extract which extracted the propolis original lump respectively in two or more sorts of ethanol water solutions in which the loadings of water differ, and was obtained.

[Claim 2] the propolis extract from which the loadings of water extracted and were obtained in the ethanol water solution of under 5 capacity % - 10 capacity %, and the propolis extract from which the loadings of water extracted and were obtained in the ethanol water solution of 45 capacity % - 55 capacity % — capacity — the antioxidation activity propolis product according to claim 1 characterized by coming to mix at a rate of 4-6:6-4 with a mixing ratio.

[Claim 3] A propolis original lump is an antioxidation activity propolis product according to claim 1 or 2 characterized by originating in eucalyptus Alecrim from Brazil.

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## DETAILED DESCRIPTION

## [Detailed Description of the Invention]

[0001]

[Field of the Invention] About a propolis product, this invention relates to the propolis product excellent in antioxidation activity while having extensive bioactive in detail.

[0002]

[Description of the Prior Art] Propolis is the resinoid originating in the vegetation which the honeybee accumulated in the blow hole of a honeybee etc. collected, the saliva of a honeybee, etc., various components, such as flavonoid, terpenoid, amino acid, a mineral, and a vitamin, are contained, and pressure of business of it is carried out as health food which can expect extensive bioactive, such as carcinostatic, antiallergic, antibacterial antiviral activity, and skin disease. Especially prevention and an improvement of lifestyle-related diseases, such as cancer it is expected to be today when a super-aged society is greeted to increase increasingly, arteriosclerosis, diabetes mellitus, a cataract, and an immunity insufficiency, are the important technical problems on national medical care, it has become clear that these lifestyle-related diseases are caused by damaging a living body cell by active oxygen in connection with aging, and in order to be prevention and an improvement of aging change, the intake of food which has antioxidation activity is encouraged.

[0003] By the way, since much impurity is included in a propolis original lump in addition to a component with bioactive, as for propolis, it is common to extract a propolis extract from a propolis original lump, and to take in with the shape of a solid and a liquefied gestalt. Conventionally, as an approach of extracting a propolis extract from a propolis original lump, there are a water extraction method, an alcoholic extraction method, and an alcoholic water-solution extraction method. Although a hydrophilic component can be extracted so much according to the water extraction method, the extract of an oleophilic component stops a little, and according to the alcoholic extraction method, although an oleophilic component can be extracted so much, the extract of a hydrophilic component stops a little. According to the alcoholic water-solution extraction method extracted with the mixed solution of alcohol and water, both a hydrophilic component and an oleophilic component can be extracted.

[0004] On the other hand, there are various reports about the bioactive of the propolis extract obtained by various extraction methods. For example, since there is a report that antiallergic is in the propolis extract obtained by a report and an alcoholic extract that carcinostatic is in the propolis extract obtained by the water extraction method, bioactive is expected from both a hydrophilic component and an oleophilic component, and according to the propolis extract by the alcoholic water-solution extraction method which can extract both, the extensive bioactive which propolis has is expected.

[0005]

[Problem(s) to be Solved by the Invention] However, there are no propolis product, therefore report sufficient until now excellent in antioxidation activity, containing extensively the bioactive component which propolis has.

[0006] Then, this invention is made in view of the above-mentioned situation, and while having the extensive bioactive which propolis has, let it be a technical problem to offer the propolis product which has antioxidation activity effective in prevention and an improvement of aging change.

[0007]

[Means for Solving the Problem] this invention persons repeated examination per antioxidation activity of the mixture of the propolis extract extracted in the alcoholic water solution in which the loadings of water differ, and hit on an idea to this invention while they paid their attention to the alcoholic water-solution extraction method. That is, it is related with the antioxidation activity propolis product characterized by this invention coming to mix the propolis extract which extracted the propolis original lump respectively in two or more sorts of ethanol water solutions in which the loadings of water differ, and was obtained (claim 1).

[0008] Since it has that the hydrophilic component and oleophilic component which are contained in propolis can be extracted, and the extensive bioactive which propolis has can be expected, and the outstanding antioxidation activity according to invention of the above-mentioned configuration, a propolis product effective in prevention and an improvement of aging change can be obtained. In addition, a propolis product here means that to which pharmaceutical preparation-ization etc. carried out the mixture itself which mixed two or more sorts of propolis extracts, or this mixture.

[0009] Moreover, the propolis extract which the loadings of water extracted the propolis original lump in the ethanol water solution of under 5 capacity % - 10 capacity %, and was obtained in invention according to claim 1, the propolis extract from which the loadings of water extracted and were obtained in the ethanol water solution of 45 capacity % - 55 capacity % - capacity -- it is related with the antioxidation activity propolis product characterized by coming to mix at a rate of 4-6:6-4 with a mixing ratio (claim 2).

[0010] Moreover, in invention according to claim 1 or 2, a propolis original lump is related with the antioxidation activity propolis product characterized by originating in eucalyptus Alecrim from Brazil (claim 3). Since the propolis product which contains the ARUTE pilin C so much is obtained according to invention of this configuration, inducing the apoptosis of a cancer cell is expected.

[0011]

[Embodiment of the Invention] The propolis original lump which becomes the raw material of a propolis extract has the desirable propolis original lump from Brazil which the honeybee assembled in this invention from the sap of eucalyptus AREKUREN which is excellent in the content of the ARUTE pilin C etc., although a honeybee becomes various [ the class of component, a content, etc. ] according to the class of tree which collects sap etc. Although ground by the crusher depending on the magnitude, as long

as a propolis original lump is a pellet, he may omit grinding.

[0012] It extracts using two or more sorts of ethanol water solutions with which the loadings of water differ in a propolis original lump. When using two sorts of ethanol water solutions with which the loadings of water differ, under 5 capacity % - 10 capacity % of the loadings of the water of one ethanol water solution is desirable, further 7 capacity % - 9 capacity % is desirable, the loadings of the water of the ethanol water solution of another side have desirable 45 capacity % - 55 capacity %, and its further 48 capacity % - 53 capacity % is desirable. As for the ethanol water solution used for an extract, it is desirable amount (ml) To use 3 times to 6 times to a propolis original lump's amount (g). Although extract operation may be performed in ordinary temperature, agitating, it is desirable to carry out by warming at 65 degrees C - 75 degrees C. Extract time amount can be suitably fluctuated, although usually considered as 1 - 3 hours.

[0013] If the above-mentioned extract operation is completed, when it warms, after cooling, when not warming, solid liquid separation will be promptly performed using a centrifugal separator, and supernatant liquor will be obtained.

[0014] Subsequently, the above-mentioned supernatant liquor is condensed by reduced pressure actuation. An excipient can be added in concentration liquid. An excipient can use what is usually used in a remedy field, for example, can mention a dextrin, corn starch, rice powder, a lactose, potatostarch, etc.

[0015] Freeze drying is presented with the above-mentioned concentration liquid, and it obtains a solid. The propolis extract by which ground the obtained solid using the hammer mill etc. and disintegration was carried out is manufactured.

[0016] Two or more sorts of propolis extracts extracted from the ethanol water solution with which the loadings of the water manufactured as mentioned above differ are mixed, and the propolis product of this invention is \*(ed). the case where the propolis extract extracted from the ethanol water solution of under 5 capacity % - 10 capacity % and the propolis extract with which the loadings of water were extracted from the ethanol water solution of 45 capacity % - 55 capacity % are mixed — the capacity of the former and the latter — it is desirable to mix so that a mixing ratio may be set to 4-6:6-4. Mixed actuation is fully performed so that both may become homogeneity.

[0017] The propolis product of this invention manufactured by the above can be used as the capsule and tablet which can use with various gestalten, for example, are usually used in a remedy field, or can also be used as liquids and solutions.

[0018]

[Example] Subsequently, although an example is given and this invention is explained, this invention is not limited to the following examples.

[0019] 1000g of the propolis original lump from Brazil originating in eucalyptus Alecrim was put in in the extract tank with an agitator, and while the loadings of water added and agitated 4000ml of ethanol water solutions of 9 capacity %, it warmed and extracted at 60 degrees C.

[0020] Subsequently, it applied to the bucket mold centrifugal separator (the Takeda machine company make) for 10,000r.p.m 15 minutes after cooling the extract obtained above, solid liquid separation was performed, and supernatant liquor was obtained. Furthermore, after carrying out vacuum concentration of the supernatant liquor, it freeze-dried by adding the rice powder of optimum dose. The obtained solid was ground using the hammer mill and the propolis extract was manufactured.

[0021] Furthermore, the propolis extract was manufactured by the same actuation as the above from the propolis original lump from Brazil with which the loadings of water originate in eucalyptus Alecrim using the ethanol water solution of 50 capacity %.

[0022] it mixed at the rate of a capacity factor which shows the propolis extract with which the loadings of the water manufactured by the above were extracted from the ethanol water solution of 9 capacity %, and the propolis extract with which the loadings of water were extracted from the ethanol water solution of 50 capacity % in a table 1, and the product made from each of an example 1 - an example 2 and the example 1 of a comparison - the example 2 of a comparison was carried out.

[0023]

[A table 1]

	エタノール水溶液の混合割合 (水の配合量 9 容量%)	エタノール水溶液の混合割合 (水の配合量 5 0 容量%)
実施例 1	4	6
実施例 2	6	4
比較例 1	2	8
比較例 2	8	2

[0024] Superoxide elimination activity was measured about each example and each example of a comparison. measurement of superoxide elimination activity — electron spin resonance (ESR) — it carried out using law and the unit (J. Biol.Chem., 244, 6049 (1969) reference) which J.M.McCord and I.Fridovich defined performed assessment. The result was shown in a table 2.

[0025]

[A table 2]

	スーパーオキシド消去活性
実施例 1	1. 9 × 1 0 <sup>3</sup> 単位
実施例 2	1. 9 × 1 0 <sup>3</sup> 単位
比較例 1	1. 7 × 1 0 <sup>3</sup> 単位
比較例 2	1. 0 × 1 0 <sup>3</sup> 単位

[0026] From a table 2, the example 1 and the example 2 had superoxide elimination activity inferior in especially the example 2 of a comparison to high superoxide elimination activity having been shown. Moreover, although the example 1 of a comparison excelled the example 2 of a comparison in superoxide elimination activity, it was inferior to which example. Even if many [ there were too few mixed rates of the propolis extract extracted in the ethanol water solution with few loadings of water than this and / too ], the data that superoxide elimination activity fell became clear.

[0027]

[Effect of the Invention] According to this invention explained in full detail above, the following effectiveness is done so. That is, further, since the propolis product of this invention is excellent also in antioxidation activity, it can offer a propolis product effective in prevention and an improvement of aging change, while it can expect extensive bioactive, such as carcinostatic

[ which propolis has ], antiallergic, antibacterial antiviral activity, and skin disease, since it fully contains a hydrophilic component and an oleophilic component.

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TECHNICAL FIELD

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PRIOR ART

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TECHNICAL PROBLEM

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## MEANS

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[0023]

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[A table 2]

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[Translation done.]

(19) 日本国特許庁 (J P)

## (12) 公開特許公報 (A)

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A23L 1/076		A23L 1/076	4B018
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A61P 39/06		A61P 39/06	

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(21) 出願番号	特願2001-113403 (P 2001-113403)	(71) 出願人	599030828 株式会社エフアイコーポレイション 岐阜県羽島郡岐南町徳田 5 丁目81番地
(22) 出願日	平成13年 4 月12日 (2001. 4. 12)	(72) 発明者	塩谷 知明 岐阜県羽島郡岐南町徳田 5 丁目81番 株式 会社エフアイコーポレイション内
		(74) 代理人	100109597 弁理士 西尾 章

最終頁に続く

(54) 【発明の名称】 抗酸化活性プロポリス製品

(57) 【要約】

【課題】 プロポリスの有する広範な生理活性を有すると共に、加齢変化の予防・改善に有効な抗酸化活性を有するプロポリス製品を提供すること。

【解決手段】 抗酸化活性プロポリス製品は、プロポリス原塊を、水の配合量が異なる2種以上のエタノール水溶液で各々抽出して得られたプロポリスエキスを混合してなり、水の配合量が5容量%～10容量%未満のエタノール水溶液で抽出して得られたプロポリスエキスと、水の配合量が45容量%～55容量%のエタノール水溶液で抽出して得られたプロポリスエキスを、容量混合比で4～6：6～4の割合で混合してもよい。また、抗酸化活性プロポリス製品は、ブラジル産のユーカリ・アレクリンに由来するプロポリス原塊を用いてもよい。

## 【特許請求の範囲】

【請求項 1】プロポリス原塊を、水の配合量が異なる 2 種以上のエタノール水溶液で各々抽出して得られたプロポリスエキスを混合してなることを特徴とする抗酸化活性プロポリス製品。

【請求項 2】水の配合量が 5 容量%～10 容量%未満のエタノール水溶液で抽出して得られたプロポリスエキスト、水の配合量が 4.5 容量%～5.5 容量%のエタノール水溶液で抽出して得られたプロポリスエキストを、容量混合比で 4～6 : 6～4 の割合で混合してなることを特徴とする請求項 1 に記載の抗酸化活性プロポリス製品。

【請求項 3】プロポリス原塊は、ブラジル産のユーカリ・アレクリンに由来することを特徴とする請求項 1 又は請求項 2 に記載の抗酸化活性プロポリス製品。

## 【発明の詳細な説明】

## 【0001】

【発明の属する技術分野】本発明は、プロポリス製品に関し、詳しくは、広範な生理活性を有すると共に抗酸化活性に優れたプロポリス製品に関する。

## 【0002】

【従来の技術】プロポリスは、蜜蜂の巣等に蓄積する蜜蜂が採集した植物や蜜蜂の唾液などに由来する樹脂状物質であり、フラボノイド、テルペノイド、アミノ酸、ミネラル、ビタミンなど多様な成分が含まれ、抗癌性、抗アレルギー性、抗菌抗ウイルス活性、皮膚疾患など広範な生理活性を期待できる健康食品として繁用されている。特に、超高齢化社会を迎えつつある今日、益々増加することが予想される癌、動脈硬化症、糖尿病、白内障、免疫機能不全症等の生活習慣病の予防・改善は国民医療上の重要な課題であり、これら生活習慣病は加齢に伴い活性酸素により生体細胞が損傷されることにより惹起されることが判明しており、加齢変化の予防・改善のためには抗酸化活性を有する食品の摂取が奨励されている。

【0003】ところで、プロポリス原塊には生理活性のある成分以外に多くの夾雑物を含むため、プロポリスはプロポリス原塊からプロポリスエキスを抽出して固形状あるいは液状の形態で摂取するのが一般的である。従来より、プロポリス原塊からプロポリスエキスを抽出する方法としては、水抽出法、アルコール抽出法及びアルコール水溶液抽出法がある。水抽出法によれば親水性成分は多量に抽出できるものの、親油性成分の抽出は少量に留まり、アルコール抽出法によれば、親油性成分は多量に抽出できるものの、親水性成分の抽出は少量に留まる。アルコールと水の混合溶液で抽出するアルコール水溶液抽出法によれば、親水性成分と親油性成分のいずれをも抽出することができる。

【0004】一方、各種抽出法により得られるプロポリスエキスの生理活性に関しては様々な報告がある。例えば、水抽出法により得られたプロポリスエキスを抗酸化性

があるとの報告やアルコール抽出により得られたプロポリスエキスを抗アレルギー性があるとの報告があることから、親水性成分と親油性成分のいずれにも生理活性が期待され、両者を抽出できるアルコール水溶液抽出法によるプロポリスエキスの抽出によれば、プロポリスの有する広範な生理活性が期待される。

## 【0005】

【発明が解決しようとする課題】しかしながら、プロポリスの有する生理活性成分を広範に含有しながら抗酸化活性に優れたプロポリス製品についてはこれまでに十分な報告がない。

【0006】そこで、本発明は上記事情に鑑みなされたものであり、プロポリスの有する広範な生理活性を有すると共に、加齢変化の予防・改善に有効な抗酸化活性を有するプロポリス製品を提供することを課題とする。

## 【0007】

【課題を解決するための手段】本発明者らは、アルコール水溶液抽出法に着目すると共に、水の配合量の異なるアルコール水溶液で抽出したプロポリスエキスの混合物の抗酸化活性につき検討を重ね本発明に想到した。すなわち、本発明は、プロポリス原塊を、水の配合量が異なる 2 種以上のエタノール水溶液で各々抽出して得られたプロポリスエキスを混合してなることを特徴とする抗酸化活性プロポリス製品に関する（請求項 1）。

【0008】上記構成の発明によれば、プロポリスに含有される親水性成分と親油性成分を抽出でき、プロポリスの有する広範な生理活性を期待できるばかりか、優れた抗酸化活性を有するので、加齢変化の予防・改善に有効なプロポリス製品を得ることができる。なお、ここでいうプロポリス製品とは、2 種以上のプロポリスエキスを混合した混合物自体又はこの混合物を製剤化等したものをいう。

【0009】また、請求項 1 に記載の発明において、プロポリス原塊を、水の配合量が 5 容量%～10 容量%未満のエタノール水溶液で抽出して得られたプロポリスエキスト、水の配合量が 4.5 容量%～5.5 容量%のエタノール水溶液で抽出して得られたプロポリスエキストを、容量混合比で 4～6 : 6～4 の割合で混合してなることを特徴とする抗酸化活性プロポリス製品に関する（請求項 2）。

【0010】また、請求項 1 又は請求項 2 に記載の発明において、プロポリス原塊は、ブラジル産のユーカリ・アレクリンに由来することを特徴とする抗酸化活性プロポリス製品に関する（請求項 3）。この構成の発明によれば、アルテピリン C を多量に含有するプロポリス製品が得られるので、癌細胞のアポトーシスを誘発することが期待される。

## 【0011】

【発明の実施の形態】プロポリスエキスの原材料となるプロポリス原塊は、蜜蜂が樹液などを集める樹木の種類

により含有成分の種類、含有量などが区々となるが、本発明ではアルテピリンCの含有量に優れるユーカリ・アレクレンの樹液などから蜜蜂が集めたブラジル産のプロポリス原塊が好ましい。プロポリス原塊はその大きさによっては粉碎器により粉碎されるが、小塊であれば粉碎を省略してもよい。

【0012】プロポリス原塊に水の配合量が異なる2種以上のエタノール水溶液を用いて抽出する。水の配合量の異なる2種のエタノール水溶液を用いる場合、一方のエタノール水溶液の水の配合量は5容量%～10容量%未満が好ましく、更には7容量%～9容量%が好ましく、他方のエタノール水溶液の水の配合量は45容量%～55容量%が好ましく、更には48容量%～53容量%が好ましい。抽出に用いるエタノール水溶液は、プロポリス原塊の量(g)に対して3倍～6倍量(ml)用いることが好ましい。抽出操作は、攪拌しながら常温で行ってもよいが65℃～75℃で加温して行うのが好ましい。抽出時間は、通常1～3時間とするが適宜増減できる。

【0013】上記の抽出操作が完了したら、加温した場合は冷却後、加温しない場合は直ちに遠心分離機を用いて固液分離を行い、上澄液を得る。

【0014】次いで、上記の上澄液を減圧操作により濃縮する。濃縮液には賦形剤を添加することができる。賦形剤は医薬分野で通常用いられるものを用いることができ、例えばデキストリン、コーンスターチ、米粉、乳糖、バレイショデンプン等を挙げることができる。

【0015】上記の濃縮液は、凍結乾燥に供せられ固形物を得る。得られた固形物は、ハンマーミル等を用いて粉碎し粉末化されたプロポリスエキスを製造される。

【0016】以上のようにして製造された水の配合量が異なるエタノール水溶液から抽出された2種以上のプロポリスエキスを混合して本発明のプロポリス製品を製する。5容量%～10容量%未満のエタノール水溶液から抽出されたプロポリスエキスと水の配合量が45容量%

～55容量%のエタノール水溶液から抽出されたプロポリスエキスを混合する場合、前者と後者の容量混合比が4～6:6～4となるように混合するのが好ましい。混合操作は、両者が均一になるように十分に行う。

【0017】上記により製造された本発明のプロポリス製品は、様々な形態で用いることができ、例えば医薬分野で通常用いられるカプセル剤や錠剤として用いたり、あるいは液剤として用いることもできる。

【0018】

【実施例】次いで、本発明を実施例を挙げて説明するが、本発明は以下の実施例に限定されるものではない。

【0019】ユーカリ・アレクレンに由来するブラジル産のプロポリス原塊の1000gを攪拌機付き抽出タンク内に入れ、水の配合量が9容量%のエタノール水溶液4000mlを加えて攪拌しながら60℃に加温して抽出した。

【0020】次いで、上記で得られた抽出液を冷却後、バケット型遠心分離機(武田機械社製)に10,000r.p.m.15分間かけ、固液分離を行い上澄液を得た。更に、上澄液を減圧濃縮した後、適量の米粉を加えて凍結乾燥を行った。得られた固形物をハンマーミルを用いて粉碎し、プロポリスエキスを製造した。

【0021】更に、水の配合量が50容量%のエタノール水溶液を用いて、ユーカリ・アレクレンに由来するブラジル産のプロポリス原塊から上記と同様の操作によりプロポリスエキスを製造した。

【0022】上記により製造された水の配合量が9容量%のエタノール水溶液から抽出されたプロポリスエキスと水の配合量が50容量%のエタノール水溶液から抽出されたプロポリスエキスを表1に示す容量比率で混合して実施例1～実施例2及び比較例1～比較例2を各々製した。

【0023】

【表1】

	エタノール水溶液の混合割合 (水の配合量9容量%)	エタノール水溶液の混合割合 (水の配合量50容量%)
実施例1	4	6
実施例2	6	4
比較例1	2	8
比較例2	8	2

【0024】各実施例と各比較例につき、スーパーオキシド消去活性を測定した。スーパーオキシド消去活性の測定は、電子スピン共鳴(ESR)法を用いて行い、評価はJ. M. McCord及びI. Fridovichが定義した単位(J. Biol. Chem., 244, 6049(1969)参照)により行った。結果は表2に示した。

【0025】

【表2】

	スーパーオキシド消去活性
実施例1	1.9×10 <sup>3</sup> 単位
実施例2	1.9×10 <sup>3</sup> 単位
比較例1	1.7×10 <sup>3</sup> 単位
比較例2	1.0×10 <sup>3</sup> 単位

【0026】表2から、実施例1と実施例2は高いスーパーオキシド消去活性を示したのに対し、特に比較例2

はスーパーオキシド消去活性が劣っていた。また、比較

例 1 は比較例 2 よりスーパーオキシド消去活性に優れていたものの、いずれの実施例よりも劣っていた。このことより、水の配合量の少ないエタノール水溶液で抽出されたプロポリスエキスの混合割合が少なすぎても多すぎてもスーパーオキシド消去活性が低下するという事実が判明した。

【0027】

【発明の効果】 上記で詳述した本発明によれば、以下の

効果を奏する。すなわち、本発明のプロポリス製品は、親水性成分と親油性成分を十分に含有するので、プロポリスの有する抗癌性、抗アレルギー性、抗菌抗ウイルス活性、皮膚疾患など広範な生理活性を期待できると共に、更に、抗酸化活性にも優れるので、加齢変化の予防・改善に有効なプロポリス製品を提供することができる。

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フロントページの続き

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